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EXAMINER
CHANG, C

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PATENT DEPARTMENT
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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ____ days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-8 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-8 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).

12. ☒ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☒ not been received ☐ been filed in parent application, serial no. _____; filed on _____

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

15. Claim 6 generic to a plurality of disclosed patentably distinct species comprising indolyl piperidines, indolyl pyrrolidines, tetrazolyl benzothiophenes, imidazolyl indoles, triazolyl indoles, tetrazolyl indoles etc.. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

Claims 1-5, 7 and 8 will be prosecuted to the extent of the elected compounds. The remaining subject matter of claims 1-5 that are not embraced by claim 6, if elected, will be subjected to further restriction.

The inventions are distinct, each from the other because of the following reasons: compounds of claim 6 do not share a common nucleus, each compound contains a distinct heterocyclic core e.g. a tetrazolyl benzothiophene rings vs an indolyl piperidinyl rings, which are so diverse that a prior art reference anticipating one compound of claim 6 would not render the same claim obvious under 35 USC 103 with respect to another compound of this claim.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of

their recognized divergent subject matter restriction for examination purposes as indicated is proper.

During a telephone conversation with Polk on June 16, 1992 a provisional election was made with traverse to prosecute the invention of example 6, first compound of p. 101, claims 1-8, triazolyl indoles. Affirmation of this election must be made by applicant in responding to this Office action. Claims 1-8, remaining subject matter are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

16. Claims 1-8 are rejected as being drawn to an improper Markush group under Judicially created doctrine on the grounds of lack of a common nucleus. According, to the CCPA in In re Harnisch 206 USPQ 300, 305 (1980), lack of a common nucleus or core is one of the criteria present that authorizes the Commissioner of Patents to restrict an application to a single

independent and distinct invention. As noted in claim 1 all elements of the formula (1) A_1, A_2, X, Y, Z, V, W, E and F are variables, therefore, no nucleus or core has been found. Further, the scope of the term "heterocyclic group" is so diverse that unlimited variations of the variables are embraced.

Further, the improper Markush group rejection under Judicially created doctrine finds antecedent basis in case law. Compare In re Swenson 56 USPQ 180; In re Ruzicka, 66 USPQ 226 and In re Winnek 73 USPQ 225.

This rejection can be overcome by deleting the non-elected inventions from the claims.

17. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide adequate teaching of how to use the compounds.

The specification as originally filed lacks description and adequate enabling support for the claimed method i.e. "A method for the treatment/or prevention of clinical conditions for which a selective agonist of 5-HT_1-like receptors is indicated".

On p. 39 of the specification, two in vitro binding tests of the claimed compounds to the 5-HT_1-like receptors are disclosed:

1. The IC_{50} of the claimed compounds for 50% in vitro displacement of 5-HT in pig caudate was below 1μM.

2. The pEL_{50} of the compounds in an in vitro against potency assay using rabbit saphenous vein is not less than 5. These evidence is insufficient to support the claimed method of treating or preventing all indications of clinical conditions of a selective agonist of 5-HT_1-like receptor. Because, it is known in the art that 5-HT_1-like receptors have many different subtype, e.g. 5-HT_{1a}, 5-HT_{1c} etc. In addition, there are peripheral 5-HT_1-like receptors. According to Martin (Arch. pharmacal. (1449) p. 111 - p. 112 left col. 1st paragraph), central 5-HT_1-like receptor subtypes are distinct and each subtype correlates to certain potency of function. Therefore, in absence of specific comparison between applicants' compound and known compound, evidence is lacking in the record for potency of function of applicants compounds. The peripheral 5-HT_1-like receptors are of ill-defined class and no correlation of these ill-defined class of peripheral 5-HT_1-like receptors to its functionality has been discussed.

Survey of the prior art of record, support can be found for only the indolyl compounds of applicants' for treating migraine (see Poenicke and EP 313397).

Claims 1-8 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

18. Claims 1-5 and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The following terms are indefinite:

"hydrocarbon" - How many carbon? Are they long chain wax like moieties which are unsuitable for pharmaceutical compounds?

"heterocyclic group" - How many hetero atom? What ring structure? How many rings? ...

"T represents = N.G" - What does this structure mean?

"aryl" - Does this term include fused aromatic rings of 20 or more? Does this term include heteroaryl?

"heterocycloalkyl, heteroaryl, heteroarylalkyl" - Are these terms the same or different from the "aryl" or "heterocyclic group" appeared in different claims" What are they?

"clinical conditions for which a selective agonist of 5-HT_1-like receptors is indicated" - What conditions are these? What guidelines are there for an artisan to identify such patients?

"a patient in need of such treatment an effective amount" -

What constitute an "effective amount"?

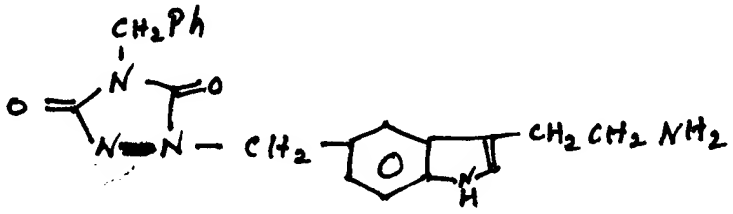
Effective against what? in whom?

19. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-8 are rejected under 35 U.S.C. § 103 as being unpatentable over Robertson EP 313397.

Robertson et al disclose triazolyl indoles for treating migraines. Compound 24 (of p. 19 lines 29) of Robertson are of the structure



The difference between Robertson's species and the elected invention is that Robertson's compound has dioxo-triazolyl ring

while applicant's compounds are triazolyl ring containing.

Generically, Robertson taught the dioxotriazolyl ring and triazolyl ring systems are choices of interchangeable moieties for these compounds (see p. 2 definition of Z and Z^1 being C=O or methylene for (iii) or (iv)).

Therefore, applicants' compounds are merely the pick-and-choose among the many compounds generically taught by Robertson. In absence of unexpected results, it is prima facie obvious to choose some among many. In re Lemin 141 USPQ 814.

20. References cited on PTO-892 to show state of the art.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is (703) 308-4702

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

C. Warren Ivy
Supervisory Patent Examiner
Group 120

CHANG:jd cc
September 10, 1992